REMARKS

Claims 1-5, 9, 23 and 27-34 are pending in this application.

I. Claims Rejection under 35 U.S.C. § 102

Claims 1, 2, 9 and 27-34 stand rejected under 35 U.S.C. § 102(e) as being allegedly unpatentable over Schafer, *et al.* (WO 2003/080049, "Schafer") (Office Action, page 6). Specifically, the Examiner alleges that Schafer discloses methods of treating various diseases, including complex regional pain syndrome, by administering the compound of the instant claims, (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione. Applicant respectfully disagrees.

The instant application claims priority to Provisional application No. 60/421,004, filed on October 24, 2002. Schafer, which was filed on March 20, 2003, claims priority to Provisional application Nos. 60/366,515 (the '515 application") and 60/438,450, filed on March 20, 2002 and January 7, 2003, respectively. Therefore, for Schafer to be prior art to the instant application under 35 U.S.C. § 102(e), the '515 application, filed earlier than the priority date of the present application, must disclose a method of treating complex regional pain syndrome using the compound of the instant claims. The '515 application does not disclose methods of treating complex regional pain syndrome, nor does it disclose methods of treating complex regional pain syndrome using the compound of the instant claims. The disclosure relied upon by the Examiner is only found in Schafer after the priority date of this application. Therefore, Schafer is not prior art to the instant claims under 35 U.S.C. § 102(e) because the earliest effective filing date of Schafer is January 7, 2003, which is after the priority date of the present application.

For these reasons, Applicant respectfully requests that the Examiner withdraw the rejection of claims 1, 2, 9 and 27-34 under 35 U.S.C. § 102(e).

II. Claims Rejections under 35 U.S.C. § 103

A. Claims 3-5 and 23 are Patentable over Schafer in view of Merck.

Claims 3-5 and 23 stand rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Schafer in view of the Merck Manual of Diagnosis and Therapy, Seventeenth Edition ("Merck") (Office Action, page 7). The Examiner alleges that the instant claims are obvious because Schafer teaches methods of treating various

diseases, including complex regional pain syndrome, by administering the compound of the instant claims, (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione, and Merck discloses that complex regional pain syndrome may be treated with certain drugs, physical therapy and/or surgery. (Office Action, page 7). Applicant respectfully disagrees.

As mentioned above, Schafer is not prior art to the instant claims because the '515 application of Schafer, which has an earlier filing date than the instant application, does not disclose methods of treating complex regional pain syndrome using the compound of the instant claims. For this reason alone, the rejection over Schafer must be withdrawn.

Even if Schafer was prior art, it does not render the claimed invention obvious for the following reasons. Even if Schafer qualifies as prior art under 35 U.S.C. § 102(e) as the Examiner contends, common ownership is sufficient to disqualify it as prior art in the § 103(a) rejection. Schafer and the instant application were commonly owned by Celgene Corporation at the time the claimed invention was made, by virtue of assignments recorded in the USPTO, and thus, Schafer is disqualified under 35 U.S.C. § 103(c). *See* Manual of Patent Examining Procedure § 706.02(l)(1) & (2) . Accordingly, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

Furthermore, Merck does not cure the defects of Schafer. Merck does not disclose or suggest methods of treating complex regional pain syndrome using the compound of the instant claims. Therefore, the references cited by the Examiner fail to teach or suggest all of the elements of the instant claims, namely, the use of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione for the treatment of complex regional pain syndrome.

The U.S. Supreme Court has recently addressed the test for obviousness under 35 U.S.C. § 103. *KSR International Co. v. Teleflex Inc.*, 127 L.Ed.2d 705, 82 U.S.P.Q.2d 1385 (2007). In *KSR,* the Supreme Court rejected the Federal Circuit's *rigid application* of the "teaching, suggestion, motivation" test ("the TSM test") in determining obviousness in the particular case in question. *Id.* at 1395. According to the Supreme Court, the correct analysis is set forth in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1 (1966). *Id.* However, the *KSR* decision indicated that while the TSM test is not the sole method for determining obviousness, it may still be used and is in some cases is helpful. *Id.* at 1396. ("When it first established [the TSM test],

the Court...captured a helpful insight."). Indeed, on May 3, 2007, the Deputy Commissioner of Patents circulated a memorandum ("USPTO Memorandum," copy enclosed) to the Technology Center Directors pointing out that the TSM test was not completely abolished in *KSR*.

The *Graham* factual inquiries, which establish a guide for determining obviousness, are: (1) determine the scope and contents of the prior art; (2) ascertain the differences between the prior art and the claims at issue; (3) resolve the level of ordinary skill in the pertinent art; and (4) evaluate any evidence of secondary considerations. *KSR,* 82 U.S.P.Q.2d at 1395 (*citing Graham,* 383 U.S. at 15-17).

The instant claims are not obvious because the references cited by the Examiner differ substantially from the subject matter of the instant claims. Moreover, the scope and content of the references cited by the Examiner do not provide any teaching, suggestion or motivation that would have prompted one of ordinary skill in the art to combine the teachings of Schafer and Merck to arrive at the methods of the instant claims.

Further, the Examiner must articulate a reason why one of ordinary skill in the art would modify these references to arrive at the methods of the instant claims. *KSR, slip op.* p. 15; *see also* USPTO Memorandum. The Examiner has not provided a reason that a person skilled in the art would have modified the teachings of the cited references. Because the Examiner has not met this burden, the instant claims are not obvious. *Id.*

B. Claims 1, 9 and 27-34 are Patentable over Omoigui in view of Muller *et al.*

Claims 1, 9 and 27-34 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Omoigui (U.S. 2004/0038874, "Omoigui") in view of Muller, *et al.* (U.S. 6,020,358, "Muller") (Office Action, page 9). Applicant respectfully disagrees.

The instant claims are not obvious because the references cited by the Examiner differ substantially from the subject matter of the instant claims. Furthermore, the scope and content of the references cited by the Examiner do not provide a reason that would have prompted one of ordinary skill in the art to combine the teachings of Omoigui and Muller to arrive at the methods of the instant claims.

1. The methods of the instant claims differ substantially from that of Omoigui in view of Muller.

In *KSR*, the Supreme Court noted the significance of the specific facts in question. Indeed, the District Court found that the invention at issue was simply a

combination of two known elements from the prior art. *KSR,* 82 U.S.P.Q.2d at 1396. Once these specific findings were made, the Court then determined whether it was obvious to combine the teaching of the prior art to arrive at the claimed invention. *Id.* Thus, the threshold issue to be resolved is the differences between the claims at issue and the prior art.

This case is not a simple combination of two known elements. Instead, the claims at issue relate to novel methods of treating complex regional pain syndrome using a specific compound, (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione, alone or in combination with another agent or therapy. The prior art must teach or suggest each element of the claims.

The Examiner alleges that claims 1, 9 and 27-34 are obvious because Omoigui teaches the use of TNF-α inhibitors, including thalidomide derivatives, to treat complex regional pain syndrome, and Muller discloses that (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione may be used to decrease levels of TNF-α in a patient. (Office Action, page 9). Applicant respectfully disagrees.

As admitted by the Examiner, Omoigui is silent as to the compound of the instant claims and its use. (Office Action, page 9). Omoigui merely discloses that thalidomide and its analogs mainly inhibit TNF- α synthesis, but the drugs also have effects on different cytokines. (Omoigui, paragraph 23). However, Omoigui does not provide any definition for or working examples to illustrate what it means by "thalidomide analogs," much less the compound recited in the instant claims. Indeed, Omoigui provides no teaching or suggestion to one skilled in the art to select the specific compound of the instant claims, much less the specific compound for the treatment of complex regional pain syndrome. Thus, Omoigui is missing essential elements of the claimed invention.[1]

[1] The focus of Omoigui is to treat pain of all kinds by mediating the inflammatory response with any of hundreds or thousands of drugs that may impact inflammation. This broad and all encompassing teaching can hardly be said to focus on thalidomide analogs. But even if it did, Omoigui provides no specific or general suggestion of any particular thalidomide analogs, not to mention the specific compound of the instant claims.

Muller does not cure the deficiency of Omoigui. Muller merely discloses that TNF-α inhibitors may be used to reduce undesirable levels of TNF-α in a patient. Muller does not disclose or suggest the use of (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione for treating complex regional pain syndrome as recited in instant claim 1.

Therefore, because substantial differences exist between the instant claims and Omoigui in view of Muller, the Examiner has provided no basis for the allegation that the instant claims are obvious over these references.

2. The teachings of Omoigui and Muller would not prompt a person of ordinary skill to combine the elements to arrive at the methods of the instant claims.

In *KSR*, the Supreme Court emphasized that the "combination of familiar elements according to known methods is likely to be obvious when it yields no more than predictable results." *KSR,* 82 U.S.P.Q.2d at 1395. However, the Court cautioned that "[f]ollowing these principles may be more difficult in other cases...because the claimed subject matter may involve more than the simple substitution of one known element for another...." *Id.* at 1396. Further, "it can be important to *identify a reason* that would have prompted a person of ordinary skill...to combine the elements in the way the claimed new invention does." *Id.* (emphasis added); *see also* USPTO Memorandum ("it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.").

As established above, the instant case involves more than the "simple substitution" of known elements in the prior art because the references cited by the Examiner do not disclose each element of the instant claims. Further, the Examiner must provide a reason why one of ordinary skill in the art would combine the teachings of Omoigui and Muller and somehow arrive at the methods of the instant claims. The Examiner has provided no reason that a person of ordinary skill would have combined the teachings of the references. The Examiner must articulate a reason why one of ordinary skill in the art would modify these references or otherwise be motivated to arrive at the methods of the instant claims. *KSR, slip op.* p. 15; *see also* USPTO Memorandum. Because the Examiner has not met this burden, the instant claims are not obvious. *Id.* Accordingly, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

C. Claims 2-5 and 23 are Patentable over Omoigui in view of Muller and Merck.

Claims 2-5 and 23 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Omoigui in view of Muller, further in view of Merck (Office Action, page 10). The Examiner alleges that the instant claims are obvious because Omoigui teaches the use of thalidomide derivatives to treat complex regional pain syndrome, Muller discloses that TNF-α inhibitors may be used to reduce undesirable levels of TNF-α in a patient, and Merck discloses that complex regional pain syndrome may be treated with certain drugs, physical therapy and/or surgery. (Office Action, pages 10-11). Applicant respectfully disagrees.

As discussed above, Omoigui in view of Muller does not teach or suggest each and every element of the instant claims. Neither Omoigui nor Muller discloses or suggests the specific compound as recited in instant claim 1 to treat complex regional pain syndrome. Merck does not cure this defect. Merck merely teaches that certain drugs, physical therapy and/or surgery may be used to treat complex regional pain syndrome. Merck does not disclose or suggest (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione for the treatment of complex regional pain syndrome. Merck does not even suggest any method of combination therapy as claimed. Therefore, the instant claims are not obvious over Omoigui in view of Muller, further in view of Merck. Accordingly, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

III. Obviousness-Type Double Patenting Rejection

Claims 1, 9 and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over either claims 1, 6, 12 and 17 of U.S. Patent No. 6,020,358 ("the '358 patent"), or claims 1, 4, 10 and 15 of U.S. Patent No. 6,011,050 ("the '050 patent"), in view of Omoigui. (Office Action, page 12). Applicant respectfully disagrees.

A. The instant claims are patentably distinct from the claims of the '358 patent in view of Omoigui.

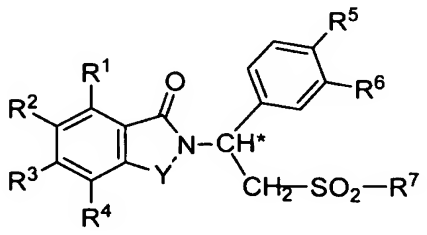
Claims 1, 6 and 12 of the '358 patent recite genuses of compounds which encompass (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione. Claim 17 of the '358 patent recites a method of reducing undesirable levels of TNF-α in a mammal using the genus of compounds recited in claim 1.

The disclosure of an earlier genus of compounds does not necessarily render obvious a subsequent claim to a species. *See In re Baird*, 16 F.3d 380, 29 USPQ2d 1550 (Fed. Cir. 1994); *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In *In re Baird*, the court held that a claim to a specific diphenol compound was not obvious over the disclosure of a genus of diphenols which encompassed the compound at issue. *In re Baird*, 16 F.3d at 383. Neither the claims of the '358 patent nor Omoigui teach or suggest the use of the specific compound of the instant claims, much less the specific compound for the treatment of complex regional pain syndrome.

The Examiner points to Omoigui to cure the defects of the '358 patent. Omoigui merely discloses the use of any compound having TNF-α activity as a possible treatment for all pain, and as mentioned above, the disclosure of an earlier genus does not necessarily render obvious a subsequent claim to a species. *Id.* Omoigui does not teach or suggest the use of the specific compound of the instant claims for the treatment of complex regional pain syndrome. Like in *In re Baird*, the claim to a species—here a method of treating complex regional pain syndrome with a specific compound—is patentable over a genus. This is particularly true here where the teaching of Omoigui is so broad and general. Thus, the instant claims are not obvious over and therefore they are patentably distinct from the claims of the '358 patent in view of Omoigui.

B. The instant claims are patentably distinct from the claims of the '050 patent in view of Omoigui.

The claims of the '050 patent recite, *inter alia*, genuses of compounds having the formula:



wherein Y is SO_2.

The instant claims are drawn to methods for treating complex regional pain syndrome using (+)-2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4-acetylaminoisoindolone-1,3-dione, which is not encompassed by the genuses of the

'050 patent because Y is SO_2. Thus, the subject matter of the instant claims is patentably distinct from the claims of the '050 patent.

The Examiner points to Omoigui to cure the defects of the '050 patent. Omoigui merely discloses the use of TNF-α inhibitors for the treatment of all pain. Omoigui does not teach or suggest the use of the specific compound of the instant claims, much less the specific compound for the treatment of complex regional pain syndrome. As mentioned above, the general teaching of Omoigui cannot render obvious the instant claims to a method of treatment of a specific disease using a specific compound. *See In re Baird*, 16 F.3d at 383. Thus, the instant claims are patentably distinct from the claims of the '050 patent in view of Omoigui.

Accordingly, Applicant respectfully requests that the double patenting rejection be withdrawn.

CONCLUSION

In view of the foregoing, all the rejections of the claims should be withdrawn. Reconsideration, entry of the above remarks, and allowance of the pending claims are respectfully requested. Should the Examiner not agree that all claims are allowable, a personal or telephonic interview is respectfully requested to discuss any remaining issues and to accelerate the allowance of the above-identified application.

No fee is believed due for this submission. However, should any fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

Respectfully submitted,

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